Theoretical Tools to Analyze Anorectal Mechanophysiological Data Generated by the Fecobionics Device

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A mechanical approach is needed for understanding anorectal function and defecation. Fecal continence is achieved by several interacting mechanisms including anatomical factors, anorectal sensation, rectal compliance, stool consistency, anal muscle strength, motility, and psychological factors. The balance is easily disturbed, resulting in symptoms such as fecal incontinence and constipation. Novel technologies have been developed in recent years for studying anorectal function. Especially, the Fecobionics device, a simulated feces, has gained attention recently. This facilitates new analysis of anorectal mechanical function. In this study, a theoretical model is developed to analyze anorectal mechanophysiological data generated by the Fecobionics device. Theoretical approaches can enhance future interdisciplinary research for unraveling defecatory function, sensory-motor disorders, and symptoms. This is a step in the direction of personalized treatment for gastrointestinal disorders based on optimized subtyping of anorectal disorders. [DOI: 10.1115/1.4044134]

Keywords: anorectal physiology, impedance planimetry, fecobionics, functional testing, modeling

1 Introduction

Inaccessibility of the gastrointestinal tract and the unavailability of gastrointestinal tissue force the modern investigator to develop new device innovations, mathematical modeling, and simulations to examine gastrointestinal sensory-motor function. Gastroenterology is an important area from a societal and clinical viewpoint, as an example, 15.3% of the U.S. population over 70 years of age and up to 9.5% below age 70 suffer from fecal incontinence [1,2]. Study of the mechanical function of the gastrointestinal tract is important as it serves to transport ingested materials and secreted fluids through the tract. Mechanical analysis including modeling and simulations requires geometric and mechanical data obtained from real tissues and experiments using advanced high-resolution technologies and imaging. New technology can advance our knowledge if it is properly applied. However, this will require a general appreciation for bioengineering, modeling, and simulation in gastroenterology.

Defecation and continence depend on several interacting mechanisms including the ability to create a high intra-abdominal pressure, colorectal motility, stool consistency, rectal capacity, rectal distensibility, anorectal sensitivity, anal muscle strength, anorectal angle, coordination of pelvic floor muscles and anal sphincter, and psychological factors [3–6]. The homeostatic balance is easily disturbed, resulting in symptoms such as fecal incontinence, constipation, or painful defecation [7–10]. Technologies are available for studying anorectal function [11]. However, the conventional technologies do not provide measurements that allow useful mechanical analysis.

This paper briefly describes conventional technologies and the Fecobionics technology. Fecobionics provides measurements that combine distension of an intraluminal bag with pressure recordings and geometric data, medical imaging based on electrical impedance measurements, three-dimensional (3D)-modeling, and new opportunities to combine data on tissue properties and luminal flow [12–14]. In this paper, we developed a theoretical model for analyzing anorectal mechanophysiological data generated by the Fecobionics device.

2 Conventional Anorectal Technologies

The conventional range of technologies available to assess anorectal function includes endoanal ultrasonography, high-resolution anorectal manometry, the balloon expulsion test (BET), defecography, and the functional luminal imaging probe (FLIP). These technologies are summarized in Table 1. They provide various measures of anorectal anatomy and function and complement each other. From a mechanical point of view, measurements such as muscle thickness, luminal diameter, and angles are useful. However, each of the technologies has limitations and does not provide detailed mechanosensory measurements during defecation under physiological circumstances. FLIP is a relatively new technology for distensibility studies of sphincters. Various distensibility parameters can be computed from the bag pressure and diameters along the anal canal recorded by FLIP during ramp distension [12,24]. In some esophagogastric junction studies, distensibility was simply evaluated as the magnitude of the cross-sectional area (CSA) or by dividing the CSA with the pressure at

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Table 1 Summary of conventional technologies for assessment of anorectal function

Technology	Purpose and assessment parameters	Limitations/disadvantages
Endoanal ultrasonography [3]	Structural assessment of anal sphincter muscle and integrity. Assessment of internal anal sphincter length, thickness, and discontinuity	No functional measurements and operator dependent. Readings of images that can be difficult to interpret
Anorectal manometry [15].	Pressure tracings or high-resolution pressure topographies for evaluation of sphincter strength, rectal sensitivity, and rectal capacity. Data are often presented as color topographies. Measurements include maximum resting pressure of the anal canal, squeeze pressure, indurance urge volume, maximal rectal capacity, and the presence of recto-anal inhibitory reflex [16]	Measurements are done during simulated defecation in front of the investigator. The procedure as well as equipment is not standardized, making comparisons of results among various centers difficult [17]
Balloon expulsion test [18]	BET is a test of simulated defecation test in which a 50 ml balloon is evacuated and the evacuation time measured	The fixed volume does not take into account the differences in size between subjects. Only measurement provided is evacuation time
Defecography (fluoroscopy or by MRI)	Defecography uses a contrast agent installed in rectum and record a video sequence during defecation. It can be used to study the anal diameter, anorectal angle, and the position of the pelvic floor at rest or during Valsalva. The completeness of evacuation, presence of rectocele, rectal intussusception, and the ability to expel rectal contents can be evaluated [19–22]. Magnetic resonance imaging technology has been added to the armamentarium of defecographic techniques [23]. It has shown excellent capabilities in diagnosing structural and functional disturbances without radiation	The three major disadvantages are the following: (1) Defecography is often done with the patient in artificial defecation position and using a paste with mechanical properties far from their usual feces (2) Extensive morphologic variability among normal healthy individuals and interobserver variability has been found [3] (3) Fluoroscopic radiation
Functional luminal imaging probe	FLIP measures the geometry of sphincteric regions during distension. This allows the measurement of various distensibility parameters	Measurements done in a fixed position, i.e., not during evacuation of the device

a given point of distension [25–27]. Needless to say, this approach may introduce bias and misinterpretation of data [12,28]. The opening pressure, the level of distension, and the actual slope of the mechanical data curves must also be taken into account [12,28]. Other studies have looked into sphincter elasticity, which has been computed as the pressure–strain modulus [29,30]

$$E_p = \frac{\Delta p}{\Delta d} \cdot d_0 \tag{1}$$

where Δp and Δd are the pressure and diameter change during the distension, respectively. d_0 is the diameter at the reference state [12,25–29]. The pressure–strain modulus is more reliable than the simple distensibility measures. Yet other studies defined a proxy of the flow resistance of the anal canal (R) during FLIP distension. This can be obtained from the anal canal length (L), the middle part diameter of the anal canal (D), and the dynamic viscosity of the inflated bag (η) as [30–32]

$$R = \frac{128 \times \eta \times L}{3.14 \times D^4} \tag{2}$$

However, more advanced technology and parameters must be considered in mechanical analysis of anorectal function [12,28].

3 Fecobionics

Limitations with the abovementioned technologies warranted the development of integrated technology that provides measures under much more physiological and pathophysiological conditions [11].

Fecobionics is a simulated stool, a bionics or biomechatronics device, that enables dynamic measurements of a variety of variables during evacuation from rectum through the anal canal [33–36]. Fecobionics imitates the defecation process in a single examination and provides manometric profiles and geometric mapping. The device has the consistency and shape of normal stool (types 3–5 on the Bristol stool scale [37]. It records pressures, CSA from electrical impedance measurements, orientation, bending, and viscoelastic properties during defecation as well as the patients can report symptoms. The device is 10 cm long and 12 mm wide with a core of medical grade resin that contains the sensors and printed circuit boards. A bag is mounted on the bendable core for distension. Sensors such as pressure transducers are placed at the front, rear, and inside the bag, two gyroscopes at the two ends for orientation and angle measurements, and impedance electrodes for CSA measurements. Fecobionics measures front and rear pressures in the direction of the flow in contrast to the radial pressure measurements in other devices. The published prototypes have been wired but wireless prototypes are now becoming available.

Fecobionics enables the measurement of high-resolution pressure and CSA profiles as well as the anorectal angle during defecation [33,34,36]. The CSA profiles are simulated in various ways, i.e., as semi-3D plots, video clips, or as color contour plots. The expulsion velocity can be assessed from changes in CSA during defecation or from data from the pressure sensors and the accelerometers. In addition to the CSA plots, promising physiological data were obtained from the pressure sensors, which allowed defecation to be divided into five distinct phases [33,34,36]. The expulsion time is comparable to that recorded with BET and the bending angle corresponds to anorectal angles reported in the literature (unpublished data). Hence, Fecobionics data are consistent with the current standards, and it integrates the current tests and provides new parameters hitherto unmeasurable.

4 New Analytical Approach to Fecobionics Measurements Based on Anorectal Tissue Deformation and Stress During Fecobionics Testing

As Fecobionics moves through the rectum and anal canal during defection, it will stress and deform anorectal tissue. Hence, computations and models that can be used to predict the tissue mechanical behavior in response to loading are important.

4.1 Geometry of the Curved Thin-Walled Shell of Revolution. The theory outlined below is borrowed from our previous study on distension in a straight hollow visceral organ [38]. However, anorectum is a hollow organ with a geometry of variable cross section and is rotationally symmetric with a curved central line. Consequently, tension calculated based on an arbitrary surface coordinate system should be used [39].

It is assumed that the Fecobionics bag and anorectum form a tube of revolution during Fecobionics movement. Furthermore, the bag size must be larger than the size of the distended anorectum to avoid pressure drop across the bag wall. The anorectal wall resists the pressure induced by the bag distension and the shear stress through the friction between the bag and the tissue wall. The given curve of the anorectal wall is called the curve of symmetry of the reference surface. The coordinates of the reference surface will be the parameter s, which determines a point on the curve of symmetry, and the angle θ, which is measured within the normal plane from the principal normal of the curve of symmetry (Fig. 1).

The curve of symmetry is defined as

$$x = x(s), \quad y = y(s), \quad z = z(s) \tag{3}$$

The unit tangent vector t is given by

$$\boldsymbol{t} = \frac{x'}{g}\boldsymbol{i} + \frac{y'}{g}\boldsymbol{j} + \frac{z'}{g}\boldsymbol{k} \tag{4}$$

where **i**, **j**, and **k** are unit vectors of x, y, and z; x', y', and z' are

$$\frac{dx}{ds}, \quad \frac{dy}{ds}, \quad \frac{dz}{ds}, \quad \text{and} \quad g = \sqrt{(x')^2 + (y')^2 + (z')^2}$$

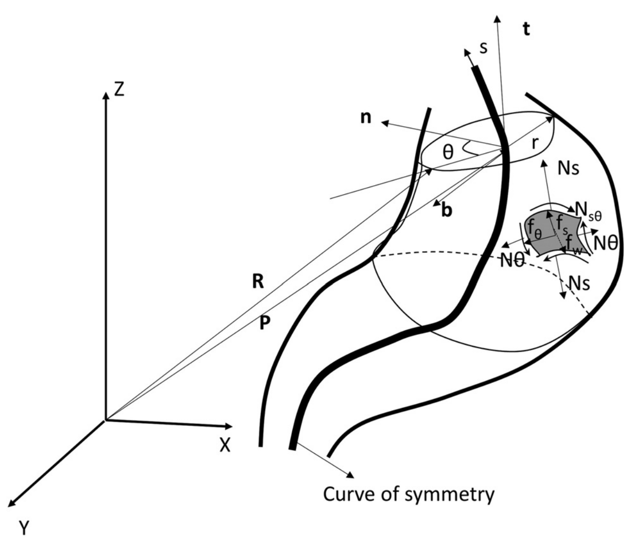

Fig. 1 Schematic diagram of a distended anorectal segment. *X*, *Y*, and *Z* are global coordinates. *S* and θ are the local coordinates with arc of length *s* along the curve of symmetry and θ the polar angle, respectively. *s* and θ form a set of curvilinear orthogonal coordinates. Membrane stress are N_θ, Ns_θ, and N_s, the circumferential, shear, and longitudinal membrane stress. The unit tangent, principal normal, and binormal vectors of the curve are t, n, and b, respectively, *R* is the position vector of a point on the reference surface, *P* is the corresponding vector of *R* at the curve of symmetry, *r* is the radius at a cross section along *s*, and f_s, f_θ, and f_w are force distribution in directions of *s*, θ, and across the wall, respectively.

The unit binormal vector **b** is defined as

$$\boldsymbol{b} = \boldsymbol{t} \times \boldsymbol{n} \tag{5}$$

where **n** is the unit principal normal.

For a continuous curve of symmetry like the center line of the anorectum, an arbitrary point on the distended bag surface with a position vector **R** can be expressed in local coordinates as (Fig. 1)

$$\boldsymbol{R}(s,\theta) = \boldsymbol{p}(s) + r(s)\cdot\cos\theta\cdot\boldsymbol{n} + r(s)\cdot\sin\theta\cdot\boldsymbol{b} \tag{6}$$

where **p** is the vector of the cross point between the cross section at s and the curve of symmetry, and r is the radius of the cross section at s. For a curved shell of revolution, the base vector along the s and θ direction of the surface can be denoted as

$$\begin{aligned} \boldsymbol{a_s} &= \frac{\partial \boldsymbol{R}}{\partial s} = g(1 - cr\cos\theta)\boldsymbol{t} + r'\cos\theta\boldsymbol{n} + r'\sin\theta\boldsymbol{b} \\ \boldsymbol{a_\theta} &= \frac{\partial \boldsymbol{R}}{\partial \theta} = -r\sin\theta\boldsymbol{n} + r\cos\theta\boldsymbol{b} \end{aligned} \tag{7}$$

where c is the circular curvature of the curve

$$c = \sqrt{n_1^2 + n_2^2 + n_3^2} \tag{8}$$

where

$$\begin{aligned} g^4 n_1 &= x''(y')^2 + x''(z')^2 - x'y'y'' - x'z'z'' \\ g^4 n_2 &= y''(z')^2 + y''(x')^2 - y'z'z'' - y'x'x'' \\ g^4 n_3 &= z''(x')^2 + z''(y')^2 - z'x'x'' - z'y'y'' \end{aligned}$$

Hence, the scale factors αs and $\alpha\theta$ can be calculated as

$$\begin{aligned} \alpha_s &= \sqrt{\boldsymbol{a_s}\cdot\boldsymbol{a_s}} = \sqrt{(g(1 - cr\cos\theta))^2 + (r')^2} \\ \alpha_\theta &= \sqrt{\boldsymbol{a_\theta}\cdot\boldsymbol{a_\theta}} = r \end{aligned} \tag{9}$$

The principal radii of curvature R_s and R_θ can be calculated as

$$\begin{aligned} R_s = {} & (\alpha_s{}^3\alpha_\theta)/\left\{rr'\left[g'(1 - cr\cos\theta) - c'gr\cos\theta - 2cgr'\cos\theta\right]\right. \\ & \left. - cg^3 r\cos\theta(1 - cr\cos\theta)^2 - grr''(1 - cr\cos\theta)\right\} \\ R_\theta = {} & \alpha_s\alpha_\theta{}^3/[gr^2(1 - cr\cos\theta)] \end{aligned} \tag{10}$$

4.2 Determination of the Membrane Tension. With the calculated geometric feature of the distended anorectal surface, the equations of equilibrium of the anorectal surface can be written as

$$\begin{aligned} & \alpha_s\frac{\partial(N_\theta)}{\partial\theta} + \frac{\partial(\alpha_\theta N_{s\theta})}{\partial s} + \frac{d\alpha_\theta}{ds}N_{s\theta} - \frac{d\alpha_s}{d\theta}(N_s - N_\theta) = -\alpha_s\cdot\alpha_\theta\cdot f_\theta \\ & \alpha_s\frac{\partial(N_{s\theta})}{\partial\theta} + \frac{\partial(\alpha_\theta N_s)}{\partial s} + 2\frac{d\alpha_s}{d\theta}N_{s\theta} - \frac{d\alpha_\theta}{ds}N_\theta = -\alpha_s\cdot\alpha_\theta\cdot f_s \\ & \frac{N_s}{R_s} + \frac{N_\theta}{R_\theta} = -f_w \end{aligned} \tag{11}$$

where f_w is the distributed force across the tissue wall, and f_s and f_θ are the distributed force (force per unit area) between Fecobionics and the wall tissue along the s and θ directions, respectively.

As that is shown in Fig. 1, the membrane stress resultants are N_s, Ns_θ, and N_θ. The boundary condition for Fecobionics in the anorectal segment is $N_s = N_{s\theta} = N_\theta = 0$ when $s \to \infty$. During Fecobionics movement, the wall is deformed and stressed by the distension, contractile force from the anorectal muscles, and the forces from Fecobionics. For anorectum, we assume that the forces across the wall, such as the bag pressure and the contractile force, are represented by the recorded bag pressure. Hence, with

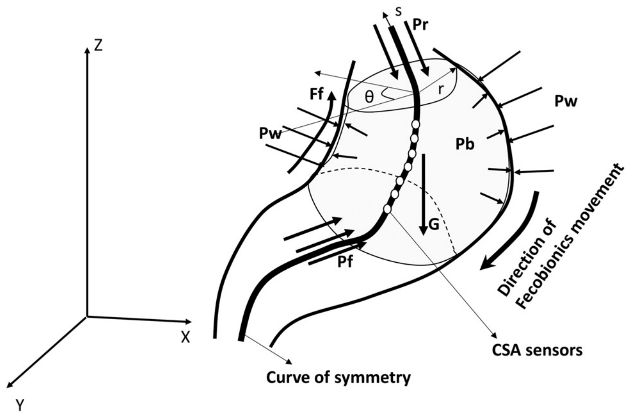

Fig. 2 Forces on Fecobionics acting on the normal and along the anorectal segment. The forces are the contractile forces from the segment (P_w), the pressure in the bag (P_b), the friction force between the device surface and the wall (F_f), the pressure from the fluid within the segment at the inlet (rear pressure, P_r), the pressure from the segment and the atmosphere at the outlet (front pressure, P_f), and also the gravity (G) of Fecobionics. X, Y, and Z are global coordinates. S and θ are the local coordinates with arc of length s along the curve of symmetry and θ the polar angle, respectively.

the estimated forces from Fecobionics, the membrane stress resultants of the anorectum can be computed as previously outlined [38].

4.3 Determination of Forces Acting on Fecobionics. For Fecobionics to move along the anorectal segment, it has to overcome a variety of forces acting on it. These forces include the contractile forces from the segment (P_w), the pressure in the bag (P_b), the friction force between the surface and the wall (F_f) [40], the pressure from the fluid within the segment at the inlet (rear pressure, P_r), the pressure from the segment and the atmosphere at the outlet (front pressure, P_f), and also the gravity (G) of Fecobionics (Fig. 2).

The pressure difference between the contractile forces in the wall and the bag distension pressure is represented by the recorded bag pressure, the rear and front pressures are recorded during Fecobionics movement, and the gravity of Fecobionics can be calculated on the basis of the volume of the inflated solution (Fig. 2). Hence, the friction force is the only unknown variable, and it can be calculated from Newton's second law with an estimated expulsion velocity along the anorectal segment as

$$\begin{aligned}\sum F_s &= \left[(-P_r + P_w)\cdot A_{\text{rear end}} + (P_f - P_w)\cdot A_{\text{front end}}\right] \\ &\quad + F_f - G_s = m\dot{v} \\ F_f &= m\dot{v} - \left\{\left[(-P_r + P_w)\cdot A_{\text{rear end}} + (P_f - P_w)\cdot A_{\text{front end}}\right] - G_s\right\}\end{aligned} \tag{12}$$

where $A_{\text{rear end}}$ and $A_{\text{front end}}$ are the surface areas of Fecobionics at both ends, m is the mass of the Fecobionics, v is the expulsion velocity of Fecobionics, $\dot{v} = dv/dt$ is the acceleration of Fecobionics moving, $\sum F_s$ the resultant force along the s direction, and G_s the gravity component in the s direction. Hence, the force distribution (force per unit area, fs, in Eq. (11)) in the s direction between the Fecobionics and the tissue can be calculated as

$$f_s = \frac{\sum F_s}{A_{\text{surface}}} \tag{13}$$

where A_{surface} is the contact surface area between the Fecobionics and the anorectal segment. In other words, the friction force can be calculated from the front and rear pressures, gravity, and the velocity during evaluation of the device.

5 The Future of Anorectal Functional Studies

Anorectal testing is directed toward high-resolution technologies that provide physiological data useful for modeling purposes. Mechanical data and models are highly needed since defecation is a mechanical event.

The Fecobionics device provides several innovative features from a bionics point of view when compared to the current anorectal assessment technologies. Such features include (a) mechanical device properties that mimic normal stool, (b) objective electronic measurement of anorectal angle independent of direction/rotation or on interpersonal interpretation of defecographic images, (c) wireless device that avoids wires and tubes that potentially could influence the mechano-sensory properties in the anorectal region, (d) pressure measurements integrated with geometric profile data and bending data, and (e) assessment of length–tension properties from the reconstructed organ shape and pressures during defecation. Fecobionics represents a disruptive technology in its infancy. It is awaiting approval by the Food and Drug Administration and hence is not yet commercially available.

It is envisaged that anatomy-based mechanophysiological models of the anorectum using data input from high-resolution integrated tests will enter the field. The present paper suggests a path for future analysis based on Fecobionics data. Profiling and modeling will have a role in future studies in the diagnosis, monitoring, and treatment of gastrointestinal diseases. This will provide better models for the Human Physiome project.[2] Recent initiatives such as the GIOME [41] and Esophagiome projects [42] will in time lead to smarter, more precise, and tailored devices and treatments.

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References

[1] Whitehead, W. E., Borrud, L., Goode, P. S., Meikle, S., Mueller, E. R., Tuteja, A., Weidner, A., Weinstein, M., and Ye, W., 2009, "Fecal Incontinence in U.S. Adults: Epidemiology and Risk Factors," Gastroenterology, **137**(2), pp. 512–517.
[2] Norton, N. J., 2004, "The Perspective of the Patient," Gastroenterology, **126**(Suppl. 1), pp. 175–179.
[3] Barleben, A., and Mills, S., 2010, "Anorectal Anatomy and Physiology," Surg. Clin., **90**, pp. 1–15.
[4] Varma, K. K., and Stephens, D., 1972, "Neuromuscular Reflexes of Rectal Continence," Aust. N. Z. J. Surg., **41**(3), pp. 263–272.
[5] Sun, W. M., Read, N. W., Prior, A., Daly, J. A., Cheah, S. K., and Grundy, D., 1990, "Sensory and Motor Responses to Rectal Distention Vary According to Rate and Pattern of Balloon Inflation," Gastroenterology, **99**(4), pp. 1008–1015.
[6] Cherry, D. A., and Rothenberger, D. A., 1988, "Pelvic Floor Physiology," Surg. Clin. North Am., **68**(6), pp. 1217–1230.
[7] Timmcke, A. E., 2007, "The ASCRS Textbook of Colon and Rectal Surgery," Ochsner J., **7**(1), p. 48.

[2]http://physiomeproject.org/

[8] Bharucha, A. E., Wald, A., Enck, P., and Rao, S., 2006, "Functional Anorectal Disorders," Gastroenterology, **130**(5), pp. 1510–1518.
[9] Rao, S. S., Bharucha, A. E., Chiarioni, G., Felt-Bersma, R., Knowles, C., Malcolm, A., and Wald, A., 2016, "Functional Anorectal Disorders," Gastroenterology, **150**(6), pp. 1430–1442.
[10] Rao, S. S., 2004, "Pathophysiology of Adult Fecal Incontinence," Gastroenterology, **126**(Suppl. 1), pp. 14–22.
[11] Palit, S., Thin, N., Knowles, C. H., Lunniss, P. J., Bharucha, A. E., and Scott, S. M., 2016, "Diagnostic Disagreement Between Tests of Evacuatory Function: A Prospective Study of 100 Consecutive Patients," Neurogastroenterol. Motil., **28**, pp. 1589–1598.
[12] Gregersen, H., and Christensen, J., 2016, *Clinical Mechanics in the Gut: An Introduction*, Bentham Science Publishers, Sharjah, United Arab Emirates.
[13] Frøkjær, J. B., Liao, D., Bergmann, A., McMahon, B. P., Steffensen, E., Drewes, A. M., and Gregersen, H., 2005, "Three-Dimensional Biomechanical Properties of the Human Rectum Evaluated With Magnetic Resonance Imaging," Neurogastroenterol. Motil., **17**, pp. 531–540.
[14] Liao, D., Frøkjær, J. B., Drewes, A. M., Gilja, O. H., Hausken, T., and Gregersen, H., 2005, *Three-Dimensional Model Analysis in the Gastrointestinal Tract*, IST Press, Lisbon, Portugal, pp. 13–24.
[15] Benezech, A., Bouvier, M., and Vitton, V., 2016, "Faecal Incontinence: Current Knowledges and Perspectives," World J. Gastrointest. Pathophysiol., **7**(1), pp. 59–71.
[16] Rao, S. S., Tuteja, A. K., Vellema, T., Kempf, J., and Stessman, M., 2004, "Dyssynergic Defecation: Demographics, Symptoms, Stool Patterns, and Quality of Life," J. Clin. Gastroenterol., **38**(8), pp. 680–685.
[17] Wald, A., Bharucha, A. E., Cosman, B. C., and Whitehead, W. E., 2014, "ACG Clinical Guideline: Management of Benign Anorectal Disorders," Am. J. Gastroenterol., **109**(8), pp. 1141–1157.
[18] Pfeifer, J., and Oliveira, L., 2006, "Anorectal Manometry and the Rectoanal Inhibitory Reflex," *Constipation*, S. D. Wexner, and G. S. Duthie, eds., Springer, London, pp. 71–83.
[19] Halligan, S., Thomas, J., and Bartram, C., 1995, "Intrarectal Pressures and Balloon Expulsion Related to Evacuation Proctography," Gut, **37**(1), pp. 100–104.
[20] Jorge, J. M., Habr-Gama, A., and Wexner, S. D., 2001, "Clinical Applications and Techniques of Cinedefecography," Am. J. Surg., **182**(1), pp. 93–101.
[21] Preston, D. M., Lennard-Jones, J. E., and Thomas, B. M., 1984, "The Balloon Proctogram," Br. J. Surg., **71**(1), pp. 29–32.
[22] Mellgren, A., Bremmer, S., Johansson, C., Dolk, A., Udén, R., Ahlbäck, S. O., and Holmström, B., 1994, "Defecography. Results of Investigations in 2,816 Patients," Dis. Colon Rectum, **37**(11), pp. 1133–1141.
[23] Kruyt, R. H., Delemarre, J. B., Doornbos, J., and Vogel, H. J., 1991, "Normal Anorectum: Dynamic MR Imaging Anatomy," Radiology, **179**(1), pp. 159–163.
[24] Gregersen, H., Kraglund, K., and Djurhuus, J. C., 1990, "Variations in Duodenal Cross-Sectional Area During the Interdigestive Migrating Motility Complex," Am. J. Physiol., **259**(1), pp. G26–G31.
[25] Lottrup, C., Gregersen, H., Liao, D., Fynne, L., Frøkjær, J. B., Krogh, K., Kunwald, P., and McMahon, B. P., 2015, "Functional Lumen Imaging of the Gastrointestinal Tract," J. Gastroenterol., **50**(10), pp. 1005–1016.
[26] Kwiatek, M. A., Pandolfino, J. E., Hirano, I., and Kahrilas, P. J., 2010, "Esophagogastric Junction Distensibility Assessed With an Endoscopic Functional Luminal Imaging Probe (EndoFLIP)," Gastrointest. Endoscopy, **72**(2), pp. 272–278.
[27] Carlson, D. A., Kou, W., Lin, Z., Hinchcliff, M., Thakrar, A., Falmagne, S., Prescott, J., Dorian, E., Kahrilas, P. J., and Pandolfino, J. E., 2018, "Normal Values of Esophageal Distensibility and Distension-Induced Contractility Measured by Functional Luminal Imaging Probe Panometry," Clin. Gastroenterol. Hepatol., **17**(4), pp. 674–681.
[28] Gregersen, H., 2002, *Biomechanics of the Gastrointestinal Tract*, Springer Verlag, London.
[29] Sørensen, G., Liao, D., Lundby, L., Fynne, L., Buntzen, S., Gregersen, H., Laurberg, S., and Krogh, K., 2014, "Distensibility of the Anal Canal in Patients With Idiopathic Fecal Incontinence: A Study With the Functional Lumen Imaging Probe," Neurogastroenterol. Motil., **26**, pp. 255–263.
[30] Haas, S., Liao, D., Gregersen, H., Lundby, L., Laurberg, S., and Krogh, K., 2017, "Increased Yield Pressure in the Anal Canal During Sacral Nerve Stimulation: A Pilot Study With the Functional Lumen Imaging Probe," Neurogastroenterol. Motil., **29**, p. e12929.
[31] Hee, L., Liao, D., Sandager, P., Gregersen, H., and Uldbjerg, N., 2014, "Cervical Stiffness Evaluated In Vivo by Endoflip in Pregnant Women," PLoS One, **9**(3), p. e91121.
[32] Haas, S., Faaborg, P., Liao, D., Laurberg, S., Gregersen, H., Lundby, L., Christensen, P., and Krogh, K., 2018, "Anal Sphincter Dysfunction in Patients Treated With Primary Radiotherapy for Anal Cancer: A Study With the Functional Lumen Imaging Probe," Acta Oncol., **57**(4), pp. 465–472.
[33] Gregersen, H., and Lo, K. M., 2018, "What Is the Future of Impedance Planimetry in Gastroenterology?," J. Neurogastroenterol. Motil., **24**(2), pp. 166–181.
[34] Gregersen, H., Krogh, K., and Liao, D., 2018, "Fecobionics: Integrating Anorectal Function Measurements," Clin. Gastroenterol. Hepatol., **16**(6), pp. 981–983.
[35] Gregersen, H., 2017, "Fecobionics: A Novel Bionic Test of Anorectal Function and Defecation," Gastroenterology, **152**(5), p. S317.
[36] Sun, D., Huang, Z., Zhuang, Z., Ma, Z., Man, L. K., Liao, D., and Gregersen, H., 2019, "Fecobionics: A Novel Bionics Device for Studying Defecation," Ann. Biomed. Eng., **47**(2), pp. 576–589.
[37] Heaton, K. W., Radvan, J., Cripps, H., Mountford, R. A., Braddon, F. E., and Hughes, A. O., 1992, "Defecation Frequency and Timing, and Stool Form in the General Population: A Prospective Study," Gut, **33**(6), pp. 818–824.
[38] Gregersen, H., Kassab, G. S., and Fung, Y. C., 2004, "Determination of Membrane Tension During Balloon Distension of Intestine," Mech. Chem. Biosyst., **1**(3), pp. 191–199.
[39] Kalnins, A., 1968, "Analysis of Curved Thin-Walled Shells of Revolution," AIAA J., **6**(4), pp. 584–588.
[40] Terry, B. S., Lyle, A. B., Schoen, J. A., and Rentschler, M. E., 2011, "Preliminary Mechanical Characterization of the Small Bowel for In Vivo Robotic Mobility," ASME J. Biomech. Eng., **133**(9), p. 091010.
[41] Gregersen, H., 2006, "The Giome Project," Neurogastroenterol. Motil., **18**(5), pp. 401–402.
[42] Gregersen, H., Liao, D., and Brasseur, J. G., 2016, "The Esophagiome: Concept, Status, and Future Perspectives," Ann. N. Y. Acad. Sci., **1380**(1), pp. 6–18.